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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/845,514	04/30/2001	K. Roger Aoki	D2929CON	3428

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EXAMINER	
FORD, VANESSA L	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 04/16/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action	Application No.	Applicant(s)	
	09/845,514	AOKI ET AL.	
	Examiner	Art Unit	
	Vanessa L. Ford	1645	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 12 March 2004 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

a) ☒ The period for reply expires *3* months from the mailing date of the final rejection.

b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☐ A Notice of Appeal was filed on _____. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.

2. ☐ The proposed amendment(s) will not be entered because:

   (a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);

   (b) ☐ they raise the issue of new matter (see Note below);

   (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

   (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____.

3. ☐ Applicant's reply has overcome the following rejection(s): _____.

4. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

5. ☒ The a)☒ affidavit, b)☐ exhibit, or c)☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: *Advisory Attachment.*

6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

7. ☒ For purposes of Appeal, the proposed amendment(s) a)☐ will not be entered or b)☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

   The status of the claim(s) is (or will be) as follows:

   Claim(s) allowed: _____.

   Claim(s) objected to: _____.

   Claim(s) rejected: *1-9,17-26,28 and 29.*

   Claim(s) withdrawn from consideration: _____.

8. ☐ The proposed drawing correction filed on _____ is a)☐ approved or b)☐ disapproved by the Examiner.

9. ☐ Note the attached Information Disclosure Statement(s)(PTO-1449) Paper No(s). _____.

10. ☐ Other: _____

Advisory Action Attachment

1. Applicant's amendment, remarks and Declaration filed under 37 CFR 1.132 filed March 12, 2004 are acknowledged.

2. The Brin Declaration filed under 37 CFR 1.132 does not overcome the rejection. Dr. Brin teaches that the use of botulinum toxin type B to treat patients with dystonia in light of the complete lack of clinical experience with botulinum toxin type B would have been foolhardy and dangerous. The Brin Declaration raises issues (i.e. safety upon administration of botulinum toxin type B) that cannot be addressed by the United States Patent and Trademark Office. It should be remembered that the claims are drawn to compositions of botulinum toxin serotypes other than serotype B to be use in a method of treating patients suffering from neuromuscular conditions or diseases. The scope of the claims encompasses the use of multiple serotypes (at least two) of botulinum toxin used to treat neuromuscular conditions and diseases. The prior art references teach the administration of multiple botulinum toxin serotypes (botulinum toxin A and botulinum toxin F, in particular) to treat patients against torticollis (a neuromuscular condition). The prior art teaches the use of other botulinum toxin serotypes in treatment because of their common and unique pharmacological action. There is nothing on the record to teach or suggest that the combination of reference does not teach the claimed invention.

Rejections Maintained

3. The rejection of claims 1-9 and 17-26 under 35 U.S.C. 112, second paragraph is maintained for the reasons of record as set forth in page 2, paragraph 4 of the previous Office Action.

Applicant urges that the claims meet all requirements under 35 U.S.C. 112.

Applicant's arguments filed March 12, 2004 have been fully considered but they are not persuasive. The recitation of "…. to control a duration of therapeutic activity of the neurotoxins" is indefinite under 112, second paragraph because it is unclear as to what applicant is referring since this "control of therapeutic activity" is not defined in the instant specification. Clarification is required.

4. The rejection of claims 1, 6, 17, 22 and 26-27 under 35 U.S.C. 103(a) is maintained for the reasons of record as set forth in pages 3-4, paragraph 5 of the previous Office Action.

Applicant urges that to establish a *prima facie* case of obviousness, three basic criteria must be met; 1) there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify a primary reference or to combine reference teachings, 2) there must be a reasonable expectation of success that the suggested combination will work and 3) the prior art references must teach or suggest all claim limitations. Applicant urges

that the Examiner has failed to point out in the prior art references the suggestion or motivation to combine two or more botulinum toxins in a composition.

Applicant's arguments filed March 12, 2004 have been fully considered but they are not persuasive. In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, Ludlow et al teach the use of a composition comprising botulinum toxin to treat torticollis (a neuromuscular condition). Ludlow et al does not teach the use of at least two botulinum toxins to treat a paints suffering from a neuromuscular condition. However, Schantz et al teach that botulinum toxin A has been used to treat patients suffering from neuromuscular conditions including torticollis. It would have been obvious of skill in the art to combine the two types of botulinum toxins taught by the prior art references into a single composition because the prior art reference have taught that both botulinum toxin A and botulinum toxin F have been successful at treating torticollis. There is nothing on the record to suggest that the combination of botulinum toxins taught by the prior art will not be effective in treating torticollis. Therefore, the prior art references as combined teach the claimed invention.

5. The rejection of claims 1, 6, 17, 22 and 26-27 under 35 U.S.C. 103(a) is maintained for the reasons of record as set forth in pages 6-7, paragraph 7 of the previous Office Action.

Applicant urges that to establish a *prima facie* case of obviousness, three basic criteria must be met; 1) there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify a primary reference or to combine reference teachings, 2) there must be a reasonable expectation of success that the suggested combination will work and 3) the prior art references must teach or suggest all claim limitations. Applicant urges that the Examiner has failed to point out in the prior art references the suggestion or motivation to combine two or more botulinum toxins in a composition.

Applicant's arguments filed March 12, 2004 have been fully considered but they are not persuasive. In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, Ludlow et al teach the use of a composition comprising botulinum toxin to treat torticollis (a neuromuscular condition). Ludlow et al does not teach the use of at least two

botulinum toxins to treat a paints suffering from a neuromuscular condition. However, Tsui et al teach that botulinum toxin A and normal saline has been used to treat patients suffering from neuromuscular conditions including torticollis. It would have been obvious of skill in the art to combine the two types of botulinum toxins taught by the prior art references into a single composition because the prior art reference have taught that both botulinum toxin A and botulinum toxin F have been successful at treating torticollis. There is nothing on the record to suggest that the combination of botulinum toxins taught by the prior art will not be effective in treating torticollis. Therefore, the prior art references as combined teach the claimed invention.

6. The rejection of claims 1-9 and 17-29 under 35 U.S.C. 103(a) is maintained for the reasons of record as set forth in pages 5-6, paragraph 6 of the previous Office Action.

Applicant urges that to establish a *prima facie* case of obviousness, three basic criteria must be met; 1) there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify a primary reference or to combine reference teachings, 2) there must be a reasonable expectation of success that the suggested combination will work and 3) the prior art references must teach or suggest all claim limitations. Applicant urges that the Examiner has failed to point out in the prior art references the suggestion or motivation to combine two or more botulinum toxins in a composition.

Applicant's arguments filed March 12, 2004 have been fully considered but they are not persuasive. In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, Ludlow et al teach the use of a composition comprising botulinum toxin to treat torticollis (a neuromuscular condition). Ludlow et al does not teach the use of at least two botulinum toxins to treat a paints suffering from a neuromuscular condition. Schantz et al teach that botulinum toxin A has been used to treat patients suffering from neuromuscular conditions including torticollis. Ludlow et al and Schantz et al combined do not teach the combinations of A and B or A and E. However, Sugiyama teaches that all seven serotypes of botulinum toxin are antigenically different but have a common and unique pharmacological action. Therefore, it would have been obvious of skill in the art to combine different combinations of botulinum toxin serotypes into a single composition because the prior art reference have taught that botulinum toxin types have been successful at treating torticollis. There is nothing on the record to suggest that combinations of botulinum toxin serotypes will not be effective in treating torticollis. Therefore, the prior art references as combined teach the claimed invention.

7. The rejection of claims 1, 6, 17, 22 and 26-27 under 35 U.S.C. 103(a) is maintained for the reasons of record as set forth in pages 5-6, paragraph 6 of the previous Office Action.

Applicant urges that to establish a *prima facie* case of obviousness, three basic criteria must be met; 1) there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify a primary reference or to combine reference teachings, 2) there must be a reasonable expectation of success that the suggested combination will work and 3) the prior art references must teach or suggest all claim limitations. Applicant urges that the Examiner has failed to point out in the prior art references the suggestion or motivation to combine two or more botulinum toxins in a composition.

Applicant's arguments filed March 12, 2004 have been fully considered but they are not persuasive. In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, Ludlow et al teach the use of a composition comprising botulinum toxin to treat torticollis (a neuromuscular condition). Ludlow et al does not teach the use of at least two botulinum toxins to treat a paints suffering from a neuromuscular condition. Schantz et

al teach that botulinum toxin A has been used to treat patients suffering from neuromuscular conditions including torticollis. Ludlow et al and Schantz et al combined do not teach the combinations of A and B or A and E. However, Sugiyama teaches that all seven serotypes of botulinum toxin are antigenically different but have a common and unique pharmacological action. Therefore, it would have been obvious of skill in the art to combine all botulinum toxin serotypes or different combinations of botulinum toxin serotypes into a single composition because the prior art reference have taught that botulinum toxin types have been successful at treating torticollis. There is nothing on the record to suggest that combinations of botulinum toxin serotypes will not be effective in treating torticollis. Therefore, the prior art references as combined teach the claimed invention.

Status of Claims

8. No claims are allowed.

Conclusion

9. Any inquiry of the general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308–0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Office Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for the Group 1600 is (703) 872-9306.

Any inquiry concerning this communication from the examiner should be directed to Vanessa L. Ford, whose telephone number is (571) 228-0857. The examiner can normally be reached on Monday – Friday from 9:00 AM to 6:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached at (571) 228–0864.

Vanessa L. Ford
Biotechnology Patent Examiner
April 5, 2004

PATRICIA A. DUFFY
PRIMARY EXAMINER